No disclosure
Objectives

- Recognize all available medical treatment options for diabetes
- Individualize treatment and glycemic target based on patient factors
- Should be able to switch to more affordable treatment regimens when cost is an issue
Case

- 74 y/o male of medical history of osteoporosis, HTN, CKD
- T2DM for more than 15 years
- Admitted to hospital with hyperglycemia and urinary incontinence
- Patient reports that he has not been taking his medication for about 3 weeks because of the cost
- On admission his RBG was 520 mg/dl and A1C 11.6
Home medications

Tresiba 70 units daily

Tradjenta 5 mg daily

Actos 45 mg daily

Patient was previously on Levemir, then switched to Tresiba, he recalls that he was switched from metformin but to Tradjenta because it's safer for kidneys. He also reports that he was on glimepiride long time ago but not sure why was discontinued. No hx of severe hypoglycemia

NKDA
Hospital course

Patient was mentally alert, was found to have UTI, admitted for IV antibiotics and rehydration, oral medication were discontinued, started on lantus 30 units and Novolog 6 units before meals in addition to correction

After 2 days patient is stable and ready for discharge

His BG was well controlled on the current insulin regimen

BMP: BG 148, BUN 26, Cr 1.5 eGFR 45
What would be the most appropriate discharge regimen

1. Continue Tresiba, Tradjenta and Actos and ask the patient to see his PCP ASAP
2. d/c Tresiba, but continue Tradjenta and Actos
3. d/c Tresiba, Tradjenta and Actos, start Novolog SS
4. d/c Tresiba, Tradjenta and Actos, start Novolin N and metformin
5. d/c Tresiba, Tradjenta and Actos, start Novolin mix 70/30 and glimepiride
The Staggering Costs of Diabetes

GROWING EPIDEMIC

Diabetes affects 30 million children and adults in the U.S. That's 1 in 11 Americans.

84 million Americans have prediabetes and are at risk for developing type 2 diabetes. 90% of them don't know they have it.

Every 21 seconds someone in the U.S. is diagnosed with diabetes.

HUMAN COSTS

African Americans and Hispanics are over 50% more likely to have diabetes than non-Hispanic whites.

People with diabetes are at higher risk of serious health complications:
- Stroke
- Blindness
- Kidney Disease
- Heart Disease
- Loss of Toes, Feet, or Legs

ECONOMIC COSTS

The total cost of diabetes and prediabetes in the U.S. is $322 billion.

The average price of insulin increased nearly 3X between 2002 and 2013.

People with diabetes have health care costs 2.3X greater than those without diabetes.

Learn more at diabetes.org
Classes of medications

Metformin
Sulfonylureas SU
Meglitinides GLN
Thiazolidindiones TZD
Alfa glucosidase inhibitors AG-i
GLP-1 agonist

DPP-4 inhibitors
SGLT-2 inhibitors
Bromocriptin
Colesevelam
Insulin
Pramlintide
# Glycemic Recommendations for Nonpregnant Adults with Diabetes

<table>
<thead>
<tr>
<th><strong>A1C</strong></th>
<th><em><em>&lt;7.0%</em> (≤53 mmol/mol)</em>*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preprandial capillary plasma glucose</strong></td>
<td>80–130 mg/dL* (4.4–7.2 mmol/L)</td>
</tr>
<tr>
<td><strong>Peak postprandial capillary plasma glucose†</strong></td>
<td>&lt;180 mg/dL* (≤10.0 mmol/L)</td>
</tr>
</tbody>
</table>

* Goals should be individualized.
† Postprandial glucose measurements should be made 1–2 hours after the beginning of the meal.
Target individualization

Approach to management of hyperglycemia:

- Patient attitude and expected treatment efforts: Highly motivated, adherent, excellent self-care capacities to Less motivated, non-adherent, poor self-care capacities.
- Risks potentially associated with hypoglycemia, other adverse events: Low to High.
- Disease duration: Newly diagnosed to Long-standing.
- Life expectancy: Long to Short.
- Important comorbidities: Absent to Few/mild to Severe.
- Established vascular complications: Absent to Few/mild to Severe.
- Resources, support system: Readily available to Limited.

American Diabetes Association Standards of Medical Care in Diabetes. Glycemic targets. Diabetes Care 2017; 40 (Suppl. 1): S48-S56
Metformin

- The first choice for oral treatment of type 2 diabetes.
- Glycemic efficacy: 1-1.5%
- Cost: ($)
- No hypoglycemia or weight gain
- Gastrointestinal side effects with initiation and high doses
- B12 deficiency is often overlooked
- Lactic acidosis is exceedingly rare
- Contraindications: GFR<30, decompensated CHF, critical illness

Sulfonylureas

- Long acting: Glimepiride and Glyburide and Short acting: glipizide
- Glycemic efficacy: 1-2%
- Cost: ($)
- Side effects includes hypoglycemia and weight gain
- Hypoglycemia risk higher with long acting
- Gliclazide or Glimipride do not appear to be associated with increased CV risk

Meglitinides

- Repaglinide (Prandin) and nateglinide (Starlix) are short-acting hypoglycemics
- **Glycemic efficacy: 0.6-2.1%**
- **Cost ($$)**
- Mechanism of action is similar to the sulfonylureas but Less risk of hypoglycemia.
- Useful for patient with allergy to SFU
- Repaglinide is principally metabolized by the liver

Thiazolidinediones

- Rosiglitazone (avandia) and pioglitazone (Actos)
- Glycemic efficacy: 0.5-1.4 %
- Cost ($$)
- Side effect: Fluid retention: prominent with concomitant insulin therapy
- Rosiglitazone might be associated with increased CV risk
- Contraindicated in NYHA III CHF
- Concerns: Macular edema, Osteoporosis, bladder cancer

Alpha-glucosidase inhibitors

- Acarbose and miglitol
- Glycemic efficacy: 0.4-0.9%
- Cost ($$)
- No hypoglycemia
- Side effects: flatulence and diarrhea

GLP-1 agonists

- Injectable Liraglutide (Victoza), Exenatide (Bydureon), dulaglutide (Trulicity), Lixisenatide (soliqua)
- Glycemic efficacy: 1%
- Cost ($$$)
- Benefits: weight reduction (approximately 1.5 to 2.5 kg over 30 week)
- (Liraglutide) appears to decrease macrovascular and microvascular complications
- Side effect: Nausea, vomiting and diarrhea
- Contraindications: h/o pancreatitis, medullary thyroid cancer, gastroparesis
- Semaglutide: CV benefits

DPP-4 inhibitors

- Sitagliptin (Januvia), saxagliptin (Onglyza), linagliptin (Tradjenta), and alogliptin (Nesina)
- Glycemic efficacy: 0.4-0.8%
- Cost ($$$)
- No weight gain or hypoglycemia
- Well tolerated
- ? Acute pancreatitis
- Cases of hepatic dysfunction (liver enzyme elevations, hepatitis) with alogliptin
- Linagliptin metabolized by liver

SGLT2-inhibitors

- Dapagliflozin (Farxiga), canagliflozin (Invokana) and emagliflozin (Jardiance)
- Glycemic efficacy: 0.4-1.1%
- Cost ( $$$ )
- Benefits: Lowers systolic BP, Weight loss, No hypoglycemia
- Empagliflozin and canagliflozin appear to improve CV outcome
- Sotagliflozin for ? T1DM
- Side effect: Increased incidence of vulvovaginal candidiasis, genital infection and UTI
- Risks: Euglycemic DKA, risk of amputation with canagliflozin

Colesevelam

- Welchol is bile acid sequestrant that lowers (LDL)
- Glycemic efficacy: 0.5%
- Cost ($$$$)
- Mechanism to improve glycemic control is uncertain.
- Side effects can include constipation, nausea, and dyspepsia.
Bromocriptine

- (Cycloset) short acting bromocriptine
- Glycemic efficacy: 0.5%
- Cost ($$$$
- The mechanism of action in reducing blood sugar is unknown.
- Common side effects include nausea, vomiting, dizziness, and headache.
Insulin preparations

[Graph showing plasma insulin levels over time with markers for Aspart, lispro, glulisine, Regular, NPH, Detemir, and Glargine.]
Basal INSULIN

- **T1DM**: TDD 0.5 units/kg/day, 40% basal, 60% prandial
- **T2DM**: Add on therapy or starting, 10 U or 0.1-0.2 U/kg administered at bedtime to be titrated

($$$) Analog long glargine (Lantus, Basaglar), detemir (Levemir), degludec (Tresiba) lower risk of hypoglycemia

($) Human Intermediate (NPH) Novolin N: twice daily, hypoglycemia
BOLUS INSULIN

- T1DM: TDD 0.5 units/kg/day, 40% basal, 60% prandial
- T2DM: Add on therapy or starting, 6 units before 1-3 meals to be titrated

- $$$ Analog rapid aspart (Novolog), lispro (Humalog), glulisine (Apidra) : 5-10 mins before meals.

- $ Human Short regular (Novolin R) : 30 mins before meals

- Ultra Rapid analog Fiasp
Premixed insulin

- Not recommended for T1DM
- Convenient with less injections per day
- Difficult to titrate and needs consistent meal plan and timing
- Premixed insulin may be administered at the largest meal once daily or at the 2 largest meals twice daily.

- $$$ Analog Intermediate (NPL, NPA) + rapid lispro (Humalog mix), aspart (Novolog mix) different 70/30, 75/25, 50/50
- ($) Human Intermediate NPH + regular 70/30 Novolin mix
- Analog long Degludec + rapid aspart (Ryzodeg)

- Switching from basal use 1:1 ratio, from basal/bolus decrease TTD by 20% , then split 50/50 vs 70/30 with breakfast and dinner to be titrated separately
U-500

- Concentrated
- Available in vials and pens
- Cost ($$)
- Severe insulin resistance: > 200 units per day or 3 U/kg/day
- TTD 60/40 before breakfast and dinner
- > 300 U/day = 40/30/30 before meals
Inhaled insulin

- Ultra rapid Afrezza
- Benefits: Needle phobia
- Cost ($$$)
- Side effects includes cough and reactive airway disease
- Contraindicated in chronic lung diseases and in smokers
- Needs PFT monitoring
Pramlintide

- Pramlintide (Symlin) is a synthetic analog of amylin that reduces postprandial blood glucose by slowing gastric emptying and promoting satiety.

- Pramlintide is only approved for use in patients also taking prandial insulin to control weight.

- Cost ($$$$$)
<table>
<thead>
<tr>
<th>Drug</th>
<th>30-day Supply</th>
<th>90-day Supply</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glimepiride 1mg</td>
<td>30 tablets</td>
<td>90 tablets</td>
<td>–</td>
</tr>
<tr>
<td>Glimepiride 2mg</td>
<td>30 tablets</td>
<td>90 tablets</td>
<td>–</td>
</tr>
<tr>
<td>Glimepiride 4mg</td>
<td>30 tablets</td>
<td>90 tablets</td>
<td>–</td>
</tr>
<tr>
<td>Glipizide 5mg</td>
<td>30 tablets</td>
<td>90 tablets</td>
<td>–</td>
</tr>
<tr>
<td>Glipizide 10mg*</td>
<td>60 tablets</td>
<td>180 tablets</td>
<td>–</td>
</tr>
<tr>
<td>Glyburide 2.5mg</td>
<td>30 tablets</td>
<td>90 tablets</td>
<td>–</td>
</tr>
<tr>
<td>Glyburide 5mg (blue)</td>
<td>30 tablets</td>
<td>90 tablets</td>
<td>–</td>
</tr>
<tr>
<td>Glyburide 5mg (green)</td>
<td>30 tablets</td>
<td>90 tablets</td>
<td>–</td>
</tr>
<tr>
<td>Glyburide, micronized 3mg</td>
<td>30 tablets</td>
<td>90 tablets</td>
<td>–</td>
</tr>
<tr>
<td>Glyburide, micronized 6mg</td>
<td>30 tablets</td>
<td>90 tablets</td>
<td>–</td>
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<tr>
<td>Metformin 500mg</td>
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<td>–</td>
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<tr>
<td>Metformin 850mg</td>
<td>60 tablets</td>
<td>180 tablets</td>
<td>–</td>
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<tr>
<td>Metformin 1000mg*</td>
<td>60 tablets</td>
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<tr>
<td>Metformin 500mg ER*</td>
<td>60 tablets</td>
<td>180 tablets</td>
<td>–</td>
</tr>
</tbody>
</table>
Novolin N

Novolin N (human insulin) is an intermediate-acting insulin including diabetes type 1 and diabetes type 2. Novolin N is any insulin brand, but less expensive biosimilar version.

Check our savings tips for co-pay cards, assistance; Medicare and insurance plans.
Start with Monotherapy unless:

- A1C is greater than or equal to 9%, consider Dual Therapy.
- A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, consider Combination Injectable Therapy (See Figure 8.2).

### Monotherapy: Metformin

<table>
<thead>
<tr>
<th>Efficacy*</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia Risk</td>
<td>Low</td>
</tr>
<tr>
<td>Weight</td>
<td>Neutral/loss</td>
</tr>
<tr>
<td>Side Effects</td>
<td>GI/lactic acidosis</td>
</tr>
<tr>
<td>Costs*</td>
<td>Low</td>
</tr>
</tbody>
</table>

If A1C target not achieved after approximately 3 months of monotherapy, proceed to 2-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

### Dual Therapy: Metformin +

<table>
<thead>
<tr>
<th>Efficacy*</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycemia Risk</td>
<td>Moderate risk</td>
</tr>
<tr>
<td>Weight</td>
<td>Gain</td>
</tr>
<tr>
<td>Side Effects</td>
<td>Hypoglycemia</td>
</tr>
<tr>
<td>Costs*</td>
<td>Low</td>
</tr>
</tbody>
</table>

If A1C target not achieved after approximately 3 months of dual therapy, proceed to 3-drug combination (order not meant to denote any specific preference — choice dependent on a variety of patient- & disease-specific factors):

### Triple Therapy: Metformin +

If A1C target not achieved after approximately 3 months of triple therapy and patient (1) on oral combination, move to basal insulin or GLP-1 RA, (2) on GLP-1 RA, add basal insulin, or (3) on optimally titrated basal insulin, add GLP-1 RA or mealtime insulin. Metformin therapy should be maintained, while other oral agents may be discontinued on an individual basis to avoid unnecessarily complex or costly regimens (i.e., adding a fourth antihyperglycemic agent).

### Combination Injectable Therapy

(See Figure 8.2)
What would be the most appropriate discharge regimen

1. Continue Tresiba, Tradjenta and Actos and ask the patient to see his PCP ASAP
2. d/c Tresiba, but continue Tradjenta and Actos
3. d/c Tresiba, Tradjenta and Actos, start Novolg SS
4. d/c Tresiba, Tradjenta and Actos, start Novolin N and metformin
5. d/c Tresiba, Tradjenta and Actos, start Novolin mix 70/30 and glimepiride
Questions are guaranteed in life
Answers aren't